atrophy along with less weight compared to WT mice. β1 Hom-Hox mice presented with same characteristics (See references 5 and 6). There was a statistically significantly difference between Hom-Pod mice versus and no difference between WT versus Hom-Hox mice for albumin/creatinine ratio (Figure 5A). BUN concentrations were numerically higher in HomPod and HomHox mice compared to WT (Figure 5B).

Figures 6A-D: The analysis of cytokines and tissue markers of protein homeostasis in CKD mice and controls. Serum cytokines (Figure 6A), relative protein expression by immunoblot (Figure 6B) and relative mRNA expression by rtPCR (Figures 6C and 6D) are depicted for wild type (WT, n = 6), hoxb7 cre mice (Hom-Hox, n = 6) and mice lacking β1 integrin in the podocytes (Hom-Pod, n = 6). Parameters are presented as mean ± SEM. There were numerical differences in serum concentrations of serum IL-6, IL-10 and TNF-α between groups although none of these differences reached statistical significance (Figure 6A). There was an overall statistically significant difference between groups when comparing 20s proteasome subunits (p = 0.009) but not with Ubiquitin (Ub) conjugates and pAKT by immunoblotting (p = 0.48 and p = 0.11, respectively). In group comparisons (Figure 6B), Ub-conjugates, 20s proteasome subunits and pAKT were highly statistically significantly elevated in Hom-Pod mice compared to WT or Hom- Hox mice (p<0.003 for all). There were no statistically significant differences in Ub, 20s proteasome subunits and pATK when comparing Hom-Hox mice versus WT mice (p > 0.0125 for all). There were overall statistically significant differences for mRNA expression of E214K, E3αI and E3αII1 by real time PCR between groups (p < 0.05 for all) (Figure 6C). In group comparisons, E214K, E3αI, and E3αII expressions were highly statistically significantly higher in Hom-Pod mice compared to WT mice (p<0.003 for all) (Figure 6C). E214K and E3αI were also statistically significantly higher in Hom-Pod mice versus Hom-Hox mice (p < 0.01 for both). E3αII1 was not different between Hom-Pod versus Hom-Hox mice. There were no statistically significant differences in when comparing E214K, E3αI and E3αII1in Hom-Hox mice versus WT mice (p > 0.0125 for all) (Figure 6C). MuRF-1 and atrogin-1 expressions were numerically higher in Hom-Pod mice compared to WT mice with atrohgin-1 reaching statistical significance only (Figure 6D).

Supplemental Figure 1: The correlation coefficients determined from spearman correlation analysis between hs-CRP and forearm muscle protein turnover components using regular scale for hs-CRP among whole study population (n=129).

Supplemental Figure 2: The rates of forearm muscle protein components according to hsCRP concentrations grouped by quintiles among non-diabetic MHD patients. We examined protein turnover markers are presented as median (interquartile range) after categorizing patients into quartiles based on their hs-CRP
values. There were statistically significant associations between hs-CRP quintiles and forearm skeletal muscle protein synthesis (S2A), protein degradation (S2B) and net forearm skeletal muscle protein balance (S3C) \((p<0.001\) for all). The unadjusted comparisons of four groups defined by hs-CRP quintiles and various skeletal muscle and whole body protein turnover components were performed using the Kruskall-Wallis test and the data are depicted as box plots.

**Supplemental Figure 3:** The correlation coefficients between hs-CRP and forearm muscle protein turnover components in non-diabetic MHD patients \((n=100)\).

Spearman correlation analysis showed an inverse (negative) correlation between hs-CRP (log scale) and forearm skeletal muscle protein synthesis (S3A) whereas a direct (positive) correlation was observed with protein degradation (S3B). The inverse (negative) correlation between hs-CRP and net protein balance was remarkably robust (S3C).

**Supplemental Figure 4:** The correlation coefficients between serum interleukin-6 (IL-6) concentrations and forearm muscle protein turnover components in MHD patients \((n=56)\). Spearman correlation analysis showed an inverse (negative) correlation between IL-6 (log scale) and forearm net skeletal muscle protein balance although this did not reach statistical significance.
Skeletal muscle protein synthesis (µg/100mL/min)

Spearman's $\rho = -0.52$

$p$-value = < 0.001

Skeletal muscle protein breakdown (µg/100mL/min)

Spearman's $\rho = 0.5$

$p$-value = < 0.001

Skeletal muscle net protein balance (µg/100mL/min)

Spearman's $\rho = -0.96$

$p$-value = < 0.001
Forearm Skeletal Muscle Protein Synthesis (µg/100mL/min)

- \( r_s = -0.49 \)
  - \( p < 0.001 \)

Forearm Skeletal Muscle Protein Breakdown (µg/100mL/min)

- \( r_s = 0.52 \)
  - \( p < 0.001 \)

Forearm Skeletal Muscle Protein Net Balance (µg/100mL/min)

- \( r_s = -0.95 \)
  - \( p < 0.001 \)